REMARKS

I. AMENDMENTS TO THE CLAIMS AND DISCUSSION OF THE INVENTION

The following claims have been amended: 1-3, 7-10, 14, 15, 17, 18, 24-30, 34 and 35. New claims 41-45 are added. Claims 36-38 are being canceled herein.

Thus, the active claims are claims 1-3, 5, 7-10, 14, 15, 17, 18, 23-35 and 39-45.

No new matter is being added with these amendments. Support for the amendments and new claims can be found at least in the specification at page 19, lines 3-6, throughout the examples (*e.g.* experimental Examples 1 and 5-10) in which efficacy of substituted benzoyl-containing peptides is demonstrated, and in the original claims.

To expedite examination, Applicants have limited claim 1 to those peptides of formula (I) that are derivatized at their N-terminus by a substituted benzoyl group.

In addition, amendments to claims 34-35, as well as new claims 41-45 further define selected embodiments of the invention as follows:

(a) Amended claim 34 is directed to a therapeutic method comprising administering to a subject a peptide, which is equivalent to the peptide claimed as a composition in amended claim 1.

(b) Amended claim 35 narrows claim 34 to two preferred substituted benzoyl groups - 4F-benzoyl and 2F-benzoyl.

(c) New claims 41 limits claim 39[1] to the "cancer" species.

(d) New claim 42 limits claim 39 to the chronic rheumatoid arthritis (CRA) species.

(e) New claims 43-45 limit their parent composition claim (claim 1), pharmaceutical composition claim (claim 15) and method of treatment claim (claim 35), respectively, to a set of **seven** peptides defined as SEQ ID NO:45, 46, and 64-68)

[1] Claim 39 reads on preventing/treating both cancer and chronic rheumatoid arthritis

II. THE RESTRICTION REQUIREMENT

According to the Action, the examiner considers that the claims define 26 patentably distinct inventions summarized in the table below along with indication of the linking claims:

Grp	Category	Peptide of formula	Claims in Group
1-9	**Linking claims**		**1-3, 5, 7-10 and 15**
1	**pharm. composition**; and method of **treating/preventing chronic RA**	X-DLys-Pro-Tyr-Arg-Cit-Cys-Arg	14, 31-32 and 18 and 39
2	**pharm. composition**	X-*D*Cit-Pro-Tyr-Arg-Cit-Cys-Arg	14 and 31
3	**pharm. composition**	X-*D*Lys-Pro-Tyr-Cit-Cit-Cys-Arg	14 and 31
4	**pharm. composition**	X-*D*Cit-Pro-Tyr-Cit-Cit-Cys-Arg	14 and 31
5	**pharm. composition**	X-*D*Glu-Pro-Tyr-Arg-Cit-Cys-Arg	14, 31, 32
6	**pharm. composition**	X-*D*Lys-Pro-Glu-Cit-Cys-Arg	14 and 31
7	**pharm. composition**	X-*D*Glu-Pro-*D*Glu-Arg-Cit-Cys-Arg	14 and 31
8	**pharm. composition**	X-*D*Glu-Pro-Tyr-*D*Glu-Cit-Cys-Arg	14 and 31
9	**pharm. composition**	X-*D*Glu-Pro-*D*Glu-Arg-Cit-Cys-Arg	14 and 31
1 and 10-26	**Linking claims**		**17**
10	method of treating **cancer**	X-*D*Lys-Pro-Tyr-Arg-Cit-Cys-Arg	18 and 33-40
11	method of treating **cancer**	X-*D*Cit-Pro-Tyr-Arg-Cit-Cys-Arg	18 and 39-40
12	method of treating **cancer**	X-*D*Lys-Pro-Tyr-Cit-Cit-Cys-Arg	18 and 39
13	method of treating **cancer**	X-*D*Cit-Pro-Tyr-Cit-Cit-Cys-Arg	18 and 39
14	method of treating **cancer**	X-*D*Glu-Pro-Tyr-Arg-Cit-Cys-Arg	18 and 39-40
15	method of treating **cancer**	X-*D*Lys-Pro-Glu-Cit-Cys-Arg	18 and 39
16	method of treating **cancer**	X-*D*Glu-Pro-*D*Glu-Arg-Cit-Cys-Arg	18 and 39
17	method of treating **cancer**	X-*D*Glu-Pro-Tyr-*D*Glu-Cit-Cys-Arg	18 and 39
18	method of treating **chronic RA***	X-*D*Glu-Pro-*D*Glu-Arg-Cit-Cys-Arg	18 and 39
19	method of treating **chronic RA**	X-*D*Cit-Pro-Tyr-Arg-Cit-Cys-Arg	18 and 39
20	method of treating **chronic RA**	X-*D*Lys-Pro-Tyr-Cit-Cit-Cys-Arg	18 and 39
21	method of treating **chronic RA**	X-*D*Cit-Pro-Tyr-Cit-Cit-Cys-Arg	18 and 39
22	method of treating **chronic RA**	X-*D*Glu-Pro-Tyr-Arg-Cit-Cys-Arg	18 and 39-40
23	method of treating **chronic RA**	X-*D*Lys-Pro-Glu-Cit-Cys-Arg	18 and 39
24	method of treating **chronic RA**	X-*D*Glu-Pro-*D*Glu-Arg-Cit-Cys-Arg	18 and 39
25	method of treating **chronic RA**	X-*D*Glu-Pro-Tyr-*D*Glu-Cit-Cys-Arg	18 and 39
26	method of treating **chronic RA**	X-*D*Glu-Pro-*D*Glu-Arg-Cit-Cys-Arg	18 and 39

* RA=rheumatoid arthritis

The Action notes that upon the indication of allowability of the linking claims, the restriction requirement as to the linked inventions **shall** be withdrawn and any claims depending from or otherwise requiring all the limitations of the allowable linking claims will be rejoined and fully examined.

A. Reasons Given for Restriction

The Examiner explains her reasoning for deciding that the indicated groups do not fall into a single inventive concept under PCT Rules 13.1 and 13.2. The alleged special technical feature of Group 1 is peptides sharing a common core of the formula

X-DLys-Pro-Tyr-Arg-Cit-Cys-Arg[2]

and a method for preventing or treating cancer or chronic rheumatoid arthritis. The Action cites Tamamura *et al.* (*Bioorg. Med. Chem.*, 1998, *6*:231-8; "TAM-1") and Tamamura *et al.* (BBRC, 1998, *253*:877-82; "TAM-2") as reading on this invention. These references allegedly teach T134 and T140 that comprise the formula X-DLys-ProTyr- Arg-Cit-Cys-Arg (citing to pg 232, Fig. 1 in TAM-1 and pg 878, Fig. 1 in TAM-2).

B. Applicants Response to the Restriction Requirement

(1) Election of Invention

In response to the Examiner's restriction requirement, which Applicants traverse (see below), Applicants elect Group 1 which is said to be claims 14, 31-32 and 18 and 39 that are described as being directed to pharmaceutical compositions and methods of treatment. (The Action notes that the method is for treating/preventing chronic rheumatoid arthritis (CRA), even though claim 39 reads on treatment of cancer and CRA.)

The linking claims for Group 1 are said to be claims 1-3, 5, 7-10 and 15. Furthermore, claim 17 links claim 1 and claims 10-26. These linking claims should be applicable here as Applicants are electing as a species, the treatment of cancer (see below). Thus Applicants believe that the claims that encompass the elected invention are claims 1-3, 5, 7-10, 14-15, 17-18, 23-28, 31-35 and 39-45.

(2) Traverse of Examiner's Position

The peptide referred to as T-140 and peptide analogs thereof have been described by some of the inventors of the present invention as well as by others, (for also, Tamamura *et al.*, WO 2002/020561). The structure of these peptides is based on the horseshoe crab self defense

[2] These residues correspond to the positions 8-14 of the peptide (*i.e.*, residues designated as A6-A7-A8-A9-A10-Cys-A11 in Formula (I). Presumably X here represente positions 1-7 as a "wild card".

peptides (tachyplesins and polyphemusins). Such peptides are generally about 14 residues in length, and have an antiparallel β-sheet structure that may be stabilized by a disulfide bridge between the two Cys residues. Thus, the amino acid composition of these peptides, as well as their secondary structure, share common technical features that contribute to their pharmacological activity. This conserved structure is represented in Formula I as defined in pending claims 1 and 17. (Note that the scope of original claims 1 and 17, as submitted in the PCT application from which the present case is based, was identical, the former being a second medical use claim and the latter a corresponding "method of treatment" claim).

The present invention discloses and claims novel peptide analogues in which the activity of the peptides is surprisingly maintained, or enhanced, upon incorporation of certain derivatizations and/or non-conservative substitutions. The novel and improved T-140 peptide analogues of the present invention may generally be divided into two subgroups (and some of the claimed embodiments include both these properties):

(i) Peptides derivatized at the N-terminal nitrogen, and

(ii) Glu-substituted peptides.

The present application discloses the unexpected discovery that derivatizing a T-140 analogue peptide at its N-terminus by addition of certain chemical groups, such as a substituted benzoyl group, renders them particularly useful for *in vivo* treatment of cancer and CRA; the peptides have superior pharmacological profiles compared to the hitherto known peptides of this family. While it was known previously that the positive charge of the T-140 analogue peptides is essential for their proper function, it was unexpected to discover that substitution of positively-charged residues at certain positions with Glu or D-Glu (negatively-charged at physiological pH), did not abolish the peptide's pharmacologic activity.

Thus, the unifying technical feature shared among the peptides of the invention resides in their common, novel N-terminal derivatizations and/or specific substitutions as noted above, and not in their C-terminal "half"– on which the Examiner has focused. In addition to these unique structural features, the peptides also share a common secondary structure, as above. Hence, different peptide species described by the Examiner as "distinct inventions" rather derive from a common inventive concept, namely that of T-140 peptide analogues with the specific derivatization at the α-amino nitrogen (*i.e.*, at the N-terminus) and/or particular amino acid substitutions. In view of the foregoing, it would be proper to rejoin the peptides which the Examiner has separated into the allegedly separate Groups, in particular, Groups 2-9. Moreover, just as Group 1 combines composition and method claims, it would be proper to rejoin Groups 10-17 with Group 1 (since the "species" of treating cancer is being elected below).

Applicants respectfully request the Examiner to reconsider the Restriction and rejoin the claims for the reasons provided above.

III. ELECTION OF SPECIES

The Action states that the application contains claims directed to more than one species of the generic invention, specifically, those divided according to the following criteria:

(i) SEQ ID NO's: 11-68;

(ii) Different diseases: cancer, breast cancer, prostate cancer, and CRA; and .

(iii) CXCR4 antagonists.

Each peptide group is said to be patentably distinct due to structural differences. Thus, according to the Action, for any invention (Group) selected, the Applicants are required to elect a single disclosed species from among (i) SEQ ID NOs 11-68, (ii) a single disclosed disease and (ii) a single disclosed CXCR4 antagonist.

Applicants are also reminded that their reply must identify the claims readable on the elected species, including any claims subsequently added. Upon the allowance of a generic claim, Applicants will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim.

The Office considers Claims 14, 18, 23-32, and 33-40 to correspond to the species listed above. Claims 1-3, 5, 7-10, 15 and 17 are considered to be generic. The Office's concludes, based on PCT Rule 13.1 and 13.2, that the species lack the same or corresponding special technical features for the following reasons:

(A) SEQ ID NO'S 11-68 contain different amino acids and N- and C-terminal compounds that make each peptide patentably distinct one from the other. Different amino acids and N- and C-terminal derivatizations would give each peptide different structure. Therefore, a search for one peptide would not lead to the other.

(B) Treatment of the different diseases claimed, namely cancer, breast cancer, prostate cancer and chromic rheumatoid arthritis are patentably distinct treatments of diseases, so that treatment of cancer would allegedly not treat CRA, and treatment of one cancer would allegedly not work for the other.

(C) CXCR4 antagonists have different structures and are therefore patentably distinct.

B. Applicant's Election of Species

Even though Applicants do not agree with the Office's reasoning above, the following species are elected for examination at this time:

(i) As a peptide species, Applicant hereby elects the derivatized peptide having the sequence SEQ ID NO:64,

4F-benzoyl-Arg-Arg-Nal-Cys-Tyr-Cit-Lys-DLys-Pro-Tyr-Arg-Cit-Cys-Arg-NH_2.

(ii) As a disease to be treated, Applicants hereby elect treatment of CANCER. [3]

(iii) As a CXCR4 antagonist, Applicants hereby elect SEQ ID NO:64.

The following claims read on the elected species: Claims 1, 2, 14, 15, 17, 18, 23, 24, 31 - 35, 39 - 41, and 43 – 45.

Applicants understand that once the elected species have been examined and found to be patentable, the search and examination will be enlarged to encompass the additional species.

III. CONCLUSION

Applicants believe they have responded fully to the Restriction/Election Requirements. Applicants respectfully request that the amended claim set be entered, and that their elections, traversals and requests be considered and granted. Applicants believe the claims are now in condition for examination and allowance, and await examination on the merits and early notification of allowance.

Respectfully submitted,
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[3] The undersigned discussed this eelection with the examiner by telephone and was given to understand that "cancer" vs. a particular ty-pe of cancer was considered to be one of the indicated species, and could therefore be elected.